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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DANG, IAN D	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/786,478	CHEN ET AL.	
	Examiner	Art Unit	
	Ian Dang	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *11-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-10 in the communication filed on 11/06/2006 is acknowledged. Applicants has further elected the GPCR135 amino acid SEQ ID NO:12. The traversal is on the ground that the GPCR135 with amino acid sequence of SEQ ID NO:13 and SEQ ID NO:15 without imposing burden to search and it is improper for the USPTO to refuse to examine that which Applicant regards as their invention. This is not found persuasive for the following reasons:

Applicant's attention is directed to MPEP 808.02 which states that "Where the related inventions as claimed are shown to be distinct under the criteria of MPEP 806.05(c-I), the examiner, in order to establish reasons for insisting upon restriction, must show by appropriate explanation one of the following: (A) Separate classification thereof: (B) A separate status in the art when they are classifiable together; (C) A different field of search." As set forth in the Restriction requirement, the separate classification established for each Group demonstrates that each distinct Group has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. Thus, the Restriction requirement is proper.

Applicant argues that no burden is placed on the examiner to consider all claims. As discussed above, the separate classification established for each Group demonstrates that each distinct Group requires a separate field of search, and a search of one Group would not reveal art on the other Groups, thus imposing a burden on the examiner. Furthermore, each group requires a non-coextensive sequence and non-patent literature search.

The requirement is still deemed proper and is therefore made FINAL. Claims 11-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b).

Claims 1-10 are pending and under examination.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-10 of the instant application conflict with claims 1-10 of Application No. 10/547,875. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

Claims 1-10 of the instant application are drawn to a receptor-ligand complex comprising a receptor component containing GPCR135 bound to the ligand relaxin3. The conflicting claims are identical to claims 1-10 in the application No. 10/547,875 and are not patentably distinct from each other because they are drawn to the same invention.

Claim Rejections - 35 USC § 101/112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The examiner is using the following definitions in evaluating the claims for utility.

"Specific" – A utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention.

"Substantial" – A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" – Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the Applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

See also the MPEP at § 2107-2107.02.

Claims 1-10 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, and credible utility or, in the alternative asserted utility or a well established utility.

Claims 1-10 are drawn to a receptor-ligand complex comprising a receptor component containing GPCR135 or an active fragment of GPCR135 bound to a ligand component containing relaxin3, wherein at least one of the receptor and ligand component is in a substantially pure form. Although Applicants have characterized the receptor-ligand complex comprising GPCR135 and relaxin3 in calcium and cAMP assays (Figures 6 and 8), Applicants have not provided support that the receptor-ligand complex causes or mediates any disorders.

The receptor-ligand complex is not supported by a specific utility because the exact function of the protein is not known. Applicants list a number of possible uses for the receptor ligand complex disclosed in the application, such as its role in CNS disorders, metabolic

disorders, feeding/drinking disorders, water and nutrient homeostasis, and endocrine disorders (page 45). But Applicants fail to assert a specific utility for the claimed receptor-ligand complex. None of the utilities is specifically linked to the receptor-ligand complex.

The asserted utility disclosed in the specification is not substantial because the disclosed uses of the protein are generally applicable to a wide variety of proteins. The receptor-ligand complex is not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. For instance, the specification discloses the receptor-ligand complex is involved in CNS disorders (page 45). However, this utility depends on the activity/function of the receptor-ligand complex, and on the elucidation of the association of diseases therewith, which are yet to be discovered through further research. The apparent need for such research indicates that the receptor ligand complex is not disclosed as to a currently available or substantial utility. Therefore the receptor-ligand complex claimed in this instant application has no known functions and therefore lacks support regarding utility.

Claims 1-10 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial, credible utility, asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112 (Written Description)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 6 are drawn to an active fragment of GPCR135 and claim 1 is drawn to an active fragment of relaxin3; the claims are thus genus claims. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claims do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the fragment and does not clearly define active fragment of GPCR135 and active fragment of relaxin3. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish sequences in the genus from for any active fragments of GPCR135 and any active fragments of relaxin3 are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, an active fragment of GPCR135 and an active fragment of relaxin3 are insufficient to describe the genus.

The written description requirement for a claimed genus' may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or

other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus for an active fragment of GPCR135 and an active fragment of relaxin3.

There is no description of the conserved regions, which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the active fragments encompassed by the limitations. Thus, no identifying characteristics or properties of the instant active fragment of GPCR135 and active fragment of relaxin3 are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 6 recite an active fragment of GPCR135 and claim 1 recites an active fragment of relaxin3. The claims are indefinite because the specification does not clearly

identify as to what fragments are encompassed by "active fragment" for either GPCR135 or relaxin3.

Thus the metes and bound of the claims cannot be determined.

Claim Rejections - 35 USC § 112 (Enablement)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include: (1) Nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the breath of the claims, (7) the quantity of experimentation needed, (8) relative skill of those in the art.

Nature of the invention and breath of the claims

The claims are drawn to a receptor-ligand complex comprising a receptor component containing GPCR135 bound to the ligand relaxin3 in a substantially pure form. In addition, the invention is not specific and substantial because the receptor-ligand complex has not been shown to be involved in any diseases. While receptor-ligand complex can affect cAMP and

calcium in cellular assays, its role is diseases remains unsubstantiated. Furthermore, the claimed invention is broad because components of the receptor-ligand complex in a substantially pure form encompass a broad range of purities.

Unpredictability and state of the art

The state of the art for the physiologic role of the receptor-ligand complex is not well characterized. Liu et al. (2003, cited in the IDS) teach that the dominant brain expression profiles of relaxin-3 and GPCR135 suggest that this ligand/receptor pair plays a role in the central nervous system. Given the fact that GPCR135 and LGR7 share a ligand but vastly different tissue expression patterns and signal via opposite transduction pathways (Gi versus Gs), we speculate that the two receptors exert different physiological functions, but perhaps in a coordinated manner orchestrated by their common ligand, relaxin 3. It is also equally as likely that GPCR135 and LGR7 mediate unrelated physiological functions but share only relaxin-3 as a ligand. Additional studies will be required to truly understand the interplay of these two receptor systems (page 50763, column 1 last paragraph to column 2 first paragraph).

In addition, Liu et al. (2005, cited in the IDS) teach that since GPCR135 mRNA and [^{125}I]R3/I5 binding sites are correlated with the expression of CRF receptor mRNA and in areas involved in processing sensory signals, the R3/GPCR135 signaling system might play a role in sensory processing, particularly under stressful circumstances (page 58, 2nd paragraph).

In view of these teachings, the physiological functions for the receptor-ligand complex are not predictable for any disorders.

The amount of direction or guidance present

Applicants' disclosure is limited to the characterization of the human receptor-ligand complex derived from GPCR135 and relaxin3. The specification does not provide guidance or direction regarding whether orthologs of relaxin3 in mouse or rat can bind to the mouse or rat orthologos of GPCR135. It may be possible that mouse or rat do not express relaxin3 or GPCR135. In addition, relaxin3 may not be able to form a ligand-receptor complex in the animals. Since Applicants have not determined the expression of mouse or rat of relaxin3 and GPCR135, ligand-receptor complex derived from mouse and rat may not be able to form.

Working Examples

The specification provides support that binding relaxin3 to PGCR135 decreases intracellular cAMP concentration in CHO-K1 cells stably expressing human GPCR135. Although Applicants have provided several examples for assaying GPCR135-relaxin activities in vitro (figures 7 and 8), the specification does not provide any examples for the involvement of the ligand receptor complex in any diseases. However, Applicants have not linked decreases of cAMP levels modulated by the relaxin-GPCR135 with any physiological relevances.

The quantity of experimentation needed

Because the claims are drawn to a receptor-ligand complex comprising a receptor component containing GPCR135 bound to the ligand relaxin3, and because Applicant's disclosure does not contain sufficient teachings to overcome the unpredictability taught in the art, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 2, 5-8, 9-10 are rejected under 35 U.S.C. 102(a) as being anticipated by Sudo et al. (Published online ahead of print on December 27, 2002, cited in the IDS).

The claims are drawn to a receptor-ligand complex comprising a receptor component of GPCR135 bound to the ligand component relaxin3. The receptor and ligand components of the ligand-receptor complex are from human, mouse, or rat and are in a substantially pure form as a product of isolation, recombinant expression, or peptide synthesis. The receptor-ligand complex is labeled with [^{125}I] radioisotope label. The receptor ligand complex is a product of expression on the cell surface of a recombinant GPCR135 host cell and is associated with isolated cell membrane or lipid vesicle.

Sudo et al. teach a receptor ligand complex comprising LGR7, also called GPCR135, binding to H3 relaxin, or relaxin 3, meeting the limitation of claim 1 (page 7855, Abstract). In addition, the ligand Relaxin3 or H3 relaxin (page 7855, column 2, 2nd paragraph) is derived from humans and the receptor GPCR135, also LGR7, (page 7855, column 2, past paragraph) is derived from humans meeting the limitation of claims 2 and 7-8. Moreover, the GPCR135 component of the receptor-ligand complex is the product of expression of cell surface of a recombinant GPCR135 in a host cell, human 293 T cells, in ligand binding assays, meeting the limitations of claim 5 (page 7856, column 2, last paragraph). Furthermore, the receptor component of GPCR135 associated with isolated cells membranes in the ligand binding analysis (figure 3, page 7358 and Table III, page 7857) meeting the limitation of claim 6.

Finally, relaxin3, the ligand of the receptor-ligand complex is a product of peptide synthesis (page 7855, column 2, 3rd paragraph) meeting the limitations of claims 9-10.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 3 are is rejected under 35 U.S.C. 103(a) as being unpatentable over Sudo et al. (Published online ahead of print on December 27, 2002, cited in the IDS) in view of Bathgate et al. (Published online ahead of print on October 31, 2001, cited in the IDS).

The claims are drawn to a receptor-ligand complex comprising a receptor component of GPCR135 bound to the ligand component relaxin3, wherein the receptor-ligand complex is labeled with [^{125}I] radioisotope label, the GPCR135 has an amino acid sequence encoded by SEQ ID NO:12, components of the receptor and ligands components are a product of isolation, peptide synthesis, or recombinant expression.

Sudo et al. teach a receptor-ligand complex comprising GPCR135 bound to relaxin 3. Sudo et al. do not explicitly teach that the receptor-ligand complex is labeled with an ^{125}I radioisotope label.Bathgate et al. teach labeling of the H2 relaxin receptor complex with [^{125}I] for a ligand binding assay for comparing the ability to characterize H2 relaxin antibody to recognize relaxin3 (Figure 4, column 1, page 1153). In the assay, H2 relaxin was able to displace ^{125}I-labeled H2 relaxin binding to the anti-H2 relaxin antibody with high specificity, but relaxin3 did not display any cross reactivity with the antibody.

It would have been obvious prima facie obvious for one of ordinary skill in the art at the time of the invention was made to label relaxin3 with the ^{125}I label taught by Bathgate et al. in the receptor-ligand complex comprising components of GPCR135 and relaxin3. One of ordinary skill in the art at the time the invention was made would have been motivated to do so because it would provide a tool to describe and characterize an additional member of the human relaxin family. Accordingly, the invention taken as a whole is prima facie obvious.

Claims 1 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sudo et al. (Published online ahead of print on December 27, 2002, cited in the IDS) in view of Borowsky et al. (US 2003/0109695 A1, filed on 2002).

The claims are drawn to a receptor-ligand complex comprising a receptor component of GPCR135 bound to the ligand component relaxin3, wherein the human GPCR135 of the receptor-ligand complex has an amino acid sequence encoded by SEQ ID NO:12.
Sudo et al. teach a receptor-ligand complex comprising GPCR135 bound to relaxin 3. Sudo et al. do not explicitly teach that the human LGR7 (also called GPCR 135) of the receptor-ligand complex is specifically encoded by SEQ ID NO:12.

Borowsky et al. teach the orphan GPCR called SNORF7 encoded by SEQ ID NO:6 (Figure 6) that has over 99% identity with GCPR135 encoded by SEQ ID NO:12 of the instant application. It belongs to the family of receptors that are characterized by a seven membrane-spanning domains and are coupled to their effectors via G-proteins linking receptor activation with intracellular stimulation of adenylyl cyclase (page 1, paragraph 003).

It would have been obvious prima facie obvious for one of ordinary skill in the art at the time of the invention was made to use the orphan GPCR taught by Borowsky et al. for the receptor-ligand complex wherein human GPCR135 has an amino acid sequence of SEQ ID

NO:12. One of ordinary skill in the art at the time the invention was made would have been motivated to do so because it would have known that the relaxin activates orphan G protein coupled receptors including SNORF7. Accordingly, the invention taken as a whole is prima facie obvious.

Conclusion

No claims are allowed.

Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ian Dang whose telephone number is (571) 272-5014. The examiner can normally be reached on Monday-Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Art Unit 1647
November 27, 2006

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